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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,470	02/24/2005	John J. Acton III	21117YP	6023

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MERCK AND CO., INC
P O BOX 2000
RAHWAY, NJ 07065-0907

EXAMINER	
LOEWE, SUN JAE Y	
ART UNIT	PAPER NUMBER
1626	

MAIL DATE	DELIVERY MODE
10/16/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/525,470	ACTON ET AL.	
	Examiner	Art Unit	
	Sun Jae Y. Loewe	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17,19,20 and 29* is/are pending in the application.

4a) Of the above claim(s) *19 and 20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,8-10,17 and 29* is/are rejected.

7)☒ Claim(s) *4-7 and 11-16* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/24/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-17, 19, 20 and 29 are pending in the instant application. Claims 18 and 21-28 were cancelled by preliminary amendment filed on February 24, 2005.

Election/Restrictions

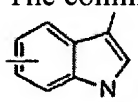
2. The subject matter of Group I (restriction requirement dated March 6, 2007) is modified to encompass the following: compounds of Formula I wherein R^3 is benzizoxazole. Group II is modified accordingly so as to exclude the subject matter of Group I.

Applicant's election with traverse of Group I in the reply received on April 4, 2007 is acknowledged. The traversal is on the ground(s):

a. " The Examiner is misapplying the explanation of the common technical feature as applied to Markush practice in MPEP§1850.III.B..... applicants' claims meet the requirements of unity of invention as defined in MPEP§1850.III.B at the bottom of page 1800-97, 2nd column, for Markush practice, where the common criteria are: (A) All alternatives have a common activity, and (B)(1) All alternatives have a common significant structural element, as described above. "

MPEP 1850.III.B. states:

> In paragraph (B)(1), above, the words "significant structural element is shared by all of the alternatives" refer to cases where the compounds share a common chemical structure which occupies a large portion of their structures, or in case the compounds have in common only a small portion of their structures, the commonly shared structure constitutes a structurally distinctive portion in view of existing prior art, and the common structure is essential to the common property or activity. The structural element may be a

The common structural element shared by *all* claimed compounds is the following core  . The other structural elements (ie. R^1-R^4) are *variables* and do not define components common to all the claimed compounds.

The indole core neither occupies a large portion of the claimed compounds (eg. see examples 2-27 on instant specification pages 33-51), nor defines a structure that is distinctive in view of the prior art (eg. Chin et al. teach compounds of the same indole core). Therefore, the claimed compounds are not of similar nature (MPEP 1850.III.B) as they do not fulfill criteria (B)(1) or (B)(2).

b. "It is therefore respectfully submitted that Chin et al has no relevance to whether applicants' claims have unity of invention."

Chin et al. teach the same core structure of the compounds instantly claimed (see above section 2a)

Applicant's arguments are not found persuasive for the reasons discussed above.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 19 and 20 withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected subject matter. Applicant timely traversed the restriction (election) requirement in the reply filed on April 3, 2007.

Information Disclosure Statement

4. The information disclosure statement (IDS) submitted on February 24, 2005 was in compliance with the provisions of 37 CFR 1.97 and 37 CFR 1.98. The IDS was considered. A signed copy of form 1449 is enclosed herewith.

Claim Objections

5. Claims 1-9, 17 and 29 objected to for containing non-elected subject matter.

6. Claims 1-17 and 29 objected to for being dependent on a base rejected/objected claim.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-3, 8-10, 17 and 29 rejected under 35 USC 112 1st paragraph as failing to comply with the written description requirement.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); In re Gostelli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

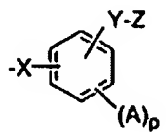
Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

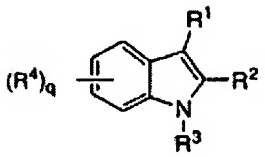
The MPEP states that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad genus. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012; 10 USPQ2d at 1618.

The Guidelines for Examination of Patent Applications Under 35 USC 112, ¶1, "Written Description" Requirement (Federal Register, Vol. 66, No. 4, pg. 1105, column 3), in accordance with MPEP § 2163, specifically state that for each claim drawn to a genus the written description requirement may be satisfied through sufficient description of a representative number of species by a) actual reduction to practice; b) reduction to drawings or structural chemical formulas; c) disclosure of relevant, identifying characteristics (ie. structure) by functional characteristics coupled with a known or disclosed correlation between function and structure. The analysis of whether the specification complies with the written description requirement calls for the examiner to compare the scope of the claim with the scope of the description to determine whether applicant has demonstrated possession of the claimed invention (Federal Register, Vol. 66, No. 4, p. 1105, 3rd column, 3rd paragraph). Below is such comparison.

I. ***Scope of Claims (based on*** elected ***subject matter)***

Compounds of Formula I wherein R^3 is benzizoxazole and R^1 is 

.



I

Variable Y-Z claimed *broader* than what is supported by the disclosure (see below section II):

II. Scope of Disclosure

Reduction to Practice:

The compounds reduced to practice support all definitions of Y-Z *except for* groups wherein:

a. Or alternatively R^7 and R^8 may be connected to form a C_3-C_6 cycloalkyl group, said C_3-C_6 cycloalkyl being optionally substituted with 1-3 halogens;

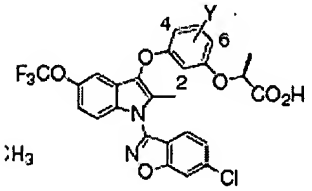
b. Or alternatively, when Y is OCR^7R^8, R^8 may optionally be a 1 carbon bridge connected to the phenyl ring at the position ortho to Y thereby yielding a 5 membered heterocyclic ring fused to the phenyl ring;

Reduction to Structural or Chemical Formulas:

There is no disclosure of species (eg. by reduction to structural/chemical formulas) in addition to those reduced to practice.

Correlation between Structure and Function:

A structure activity study is disclosed by Liu et al. for a limited subgenus of the Markush group instantly claimed. This study addresses the effect on activity upon variation of Y for the following core structure:



The disclosure does not address the SAR commensurate in scope with the structural broadness instantly claimed for "-Y-Z". Nonetheless, the disclosure suggests that the activity is influenced by the nature of this substituent. The instant specification does not provide further guidance and/or a structure activity correlation. Therefore, it is not

understood what *specific structural elements* (pertaining to variable Y-Z) are *essential* for the activity of the instantly claimed compounds (see further discussion below section 8).

III. *Analysis of Fulfillment of Written Description Requirement:*

In the absence of a correlation between structure and function, it is not possible to know what modifications to the instantly claimed core structure will allow for the preservation of the desired activity. For example, one of ordinary skill cannot predict whether the activity will be preserved upon changing variable Y-Z to result in a ring structure that is unrepresented by the instant disclosure.

In conclusion: (i) substantial structural variation exists in the genus/subgenus embraced by claims 1-3, 8-10, 17 and 29; (ii) disclosure of species supporting genus is limited to compounds reduced to practice, which scope is not commensurate with the scope of genus/subgenus claimed; (iii) common structural attributes of the claimed genus/subgenus, combined with a correlation between structure and function, is neither disclosed in the instant application nor commonly known in the art. Thus, the specification fails to provide adequate written description for the genus of compounds claimed and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

(Enablement)

8. Claims 1-3, 8-10, 17 and 29 rejected under 35 U.S.C. 112, first paragraph. The specification is enabling for making and using compounds that have adequate written description. The specification is not enabling for using compounds that are not supported by the disclosure, as the only utility disclosed is that towards PPAR receptor. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with the claims.

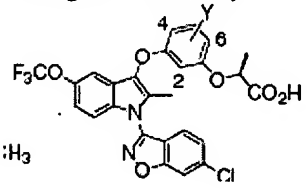
The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8USPQ2s 1400, 1404 (Fed. Cir. 1988). MPEP 2164.01(a) states "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue". The factors are applied below to the instant claims.

The breadth of the claims
Claims drawn to compounds that *do not* have written description support (see Section 7).

The nature of the invention
The compounds are disclosed to be agonists of PPARγ (instant specification page 4).

The state of the prior art/level of ordinary skill/level of predictability
The level of ordinary skill is high, but the level of predictability in the art is low. The binding ability and activity of a compound towards a receptor depends on the interaction between the chemical groups/moieties of the compound with specific residues in the binding pocket of the protein/receptor. It is well documented in the art that changes to the structure/chemical properties of a compound can have unpredictable results on its overall binding and/or functional binding ability. Studies suggest that this is the case with the PPARγ receptor, note illustrative example below:

- Liu et al (p. 2438, Table 1): SAR studies of PPARγ receptor agonists of the structure below disclosed that varying the Y substituent leads to substantial changes in activity.



The example above is provided to illustrate inability to predict activity and/or binding of a compound to the PPARγ receptor, since modest structural changes effect differences in activity.

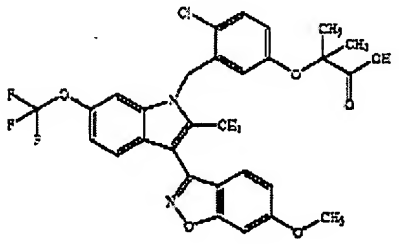
As discussed in section 7, it is not known what specific structural limitations are required for the activity of the instantly claimed genus of compounds as PPARγ agonists. In the absence of further guidance and/or structure-activity correlation, in view of the unpredictability, one of ordinary skill would not know which of the structural modifications within the instantly claimed genus of compounds would result in retention of activity. One of ordinary skill could not predict which of the structurally diverse compounds, embraced by the claims but not exemplified/supported by the disclosure, would possess the desired activity. Lacking use as PPARγ agonists, in view of the absence of an alternate utility, one of ordinary skill is not enabled by the disclosure to use the compounds which do not have written description support.

The amount of direction provided by the inventor/existence of working examples
No direction or working examples.

The quantity of experimentation needed to make or use the invention
It is not known which of the unrepresented compounds meet the structural requirement for activity as agonists of the PPARγ receptor. It would require undue experimentation for one of ordinary skill to use the full scope of compounds claimed.

Allowable Subject Matter

9. The elected subject matter is novel and unobvious over the art of record. The closest art is the disclosure of Acton et al. (US 7186746), for example, compound 39 on column 137:



The compound above neither anticipates nor makes obvious the instant invention. Moreover, the reference does not qualify as prior art under 35 USC 102.

Conclusion

10. No claims allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sun Jae Y. Loewe whose telephone number is (571) 272-9074. The examiner can normally be reached on M-F 7:30-5:00 Est.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571)272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sun Jae Y. Loewe
Art Unit 1626

REBECCA ANDERSON
PRIMARY EXAMINER